Replaces VHA Directive 98-039

Department of Veterans Affairs
Veterans Health Administration
Washington, DC 20420

VHA DIRECTIVE 99-046

October 12, 1999

INFLUENZA VACCINE - RECOMMENDATION FOR 1999-2000

1. PURPOSE: This Veterans Health Administration (VHA) Directive provides guidance on the use of the influenza vaccine for 1999-2000.

2. BACKGROUND

a. For several years the Department of Veterans Affairs (VA) has provided influenza vaccine to high-risk patients and to employees. Information is provided on vaccine composition, usage (including high-risk groups), contraindications, side effects and adverse reactions, dosage, and related preventive strategies (see Att. A). The program will continue to receive increased emphasis as a part of the VA Preventive Medicine Program, and will be assessed based on doses dispensed.

b. Influenza vaccine for 1999-2000 contains antigens of three virus strains (two type A and one type B) representing the influenza viruses that are likely to circulate in the United states in the upcoming winter. The trivalent influenza vaccine prepared for the 1999-2000 season will include A/Beijing/262/95-like (H1N1), A/Sydney/5/97-like (H3N2), and B/Beijing/184/93-like hemagglutinin antigens. For the B/Beijing/184/93-like antigen, United States manufacturers will use the antigenically-equivalent B/Yamanashi/166/98 virus because of its growth properties and because it is representative of currently circulating B viruses.

3. POLICY: It is the VHA policy to publish annual recommendations on the use of the influenza vaccine.

4. ACTION

a. VHA Headquarters recommends that the immunization program outlined by the Advisory Committee on Immunization Practices and published in Morbidity and Mortality Weekly Report (MMWR), April 30, 1999, Vol.48, No. (RR-04);1-28, be followed by VA health care facilities.

b. VA Form 10-5549, Influenza Vaccine Consent Form, (see Att. B) is to be completed by all employees receiving influenza vaccine. These forms should be locally reproduced. The forms may be used for patients as a local option, but written, informed consent is not required when the vaccine is administered in the context of a regular "practitioner-patient" relationship.

5. REFERENCES

a. Centers for Disease Control and Prevention (CDC). Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, April 30, 1999, Vol. 48, No.(RR-04); 1-28.

b. Physicians' Desk Reference, 53rd Edition. Ronald Arky, Medical Consultant. Medical Economics Co., Inc. Product Information, Wyeth-Ayerst Laboratories, 3315-3317, 1999.

THIS VHA DIRECTIVE EXPIRES OCTOBER 12, 2000

6. FOLLOW-UP RESPONSIBILITY: Chief, Patient Care Services Officer (11) is responsible for the contents of this Directive. Questions relating to the clinical aspects of the influenza immunization program should be referred to the Office of the Program Director for Infectious Diseases, Gary A. Roselle, M.D., at FTS 700-773-6398 or commercial number 513-475-6398.

7. RESCISSION: VHA Directive 98-039 is rescinded. This Directive will expire on October 12, 2000.

S/Melinda L. Murphy for
Thomas L. Garthwaite, M.D.
Acting Under Secretary for Health

Attachments

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ATTACHMENT A

INFORMATION ABOUT THE INFLUENZA VIRUS VACCINE FOR 1999-2000

1. Vaccine Use. The following groups of persons are especially targeted for vaccination:

a. Persons at High Risk for Influenza-Related Complications

(1) Persons aged 65 years or older.

(2) Residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions.

(3) Adults who have chronic disorders of the pulmonary or cardiovascular systems, including asthma.

(4) Adults who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications).

(5) Women who will be in the second or third trimester of pregnancy during the influenza season.

b. Persons Who Can Transmit Influenza to Those at High Risk

(1) Physicians, nurses, and other personnel in both hospital and outpatient-care settings.

(2) Employees of assisted living and other residences for persons in high-risk groups.

(3) Employees of nursing homes and chronic-care facilities who have contact with patients or residents.

(4) Providers of home care (e.g., visiting nurses and volunteer workers) to persons in high-risk groups

(5) Household members of persons in high-risk groups.

c. Vaccination of Other Groups.

(1) Persons Infected with Human Immunodeficiency Virus (HIV)

(a) Limited information exists regarding the frequency and severity of influenza illness or the benefits of influenza vaccination among HIV-infected persons, but reports suggest that symptoms might be prolonged and the risk for complications increased for some HIV-infected persons. Of note, a recent retrospective study of young and middle-aged women found that the attributable risk for cardiopulmonary hospitalizations among women with HIV infection was

higher during influenza seasons than in the peri-influenza periods. The risk of hospitalization for HIV-infected women was higher than the risk for women with other well-recognized high-risk conditions for influenza complications, including chronic heart and lung diseases. Other reports suggest that influenza symptoms might be prolonged and the risk for complications from influenza increased for some HIV-infected persons. Influenza vaccine has produced substantial antibody titers against influenza in vaccinated HIV-infected persons who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts. In patients who have advanced HIV disease and low CD4+ T-lymphocyte cell counts, however, influenza vaccine might not induce protective antibody titers; a second dose of vaccine does not improve the immune response for these persons.

(b) One study found that HIV RNA levels increased transiently in one HIV-infected patient after influenza infection. Some studies have demonstrated a transient (i.e., 2- to 4-week) increase in replication of HIV-1 in the plasma or peripheral blood mononuclear cells of HIV-infected persons after vaccine administration. Other studies using similar laboratory techniques have not documented a substantial increase in the replication of HIV. Deterioration of CD4+ T-lymphocyte cell counts and progression of HIV disease have not been demonstrated among HIV-infected persons who receive vaccine. The effect of antiretroviral therapy on potential increases in HIV RNA levels following either natural influenza infection or influenza vaccination is unknown.

(c) Influenza vaccine does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.

(d) Because influenza can result in serious illness and complications and because influenza vaccination can result in the production of protective antibody titers, vaccination will benefit many HIV-infected patients, including HIV-infected pregnant women.

(2) Travelers

(a) The risk for exposure to influenza during travel depends on time of year and destination. In the tropics, influenza can occur throughout the year; in the Southern Hemisphere, most activity occurs from April through September. In temperate climate zones of the Northern and Southern Hemispheres, travelers also can be exposed to influenza during the summer, especially when traveling as part of large organized tourist groups containing persons from areas of the world where influenza viruses are circulating.

(b) Persons at high risk for complications of influenza should consider receiving influenza vaccine before travel if they were not vaccinated with influenza vaccine during the preceding fall or winter and they plan to a) travel to the tropics; b) travel with large organized tourist groups at any time of year; or c) travel to the Southern Hemisphere from April through September. Persons at high risk who received the previous season's vaccine before travel should be revaccinated with the current vaccine in the following fall or winter.

(c) Because influenza vaccine might not be available during the summer in North America, persons aged greater than or equal to 65 years and others at high risk might wish to consult with

their physicians before embarking on travel during the summer to discuss the symptoms and risks of influenza and advisability of carrying antiviral medications for either prophylaxis or treatment for influenza.

(3) General Population. Physicians should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza. Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings (i.e., dormitories, domiciliaries) should be encouraged to receive vaccine to minimize disruption of routine activities during epidemics.

(4) Pregnant Women. Influenza-associated excess mortality among pregnant women has not been documented except during the pandemic of 1918-19 and 1957-58. Case reports and limited studies also suggest that pregnancy can increase the risk for serious medical complications of influenza as a result of increases in heart rate, stroke volume, and oxygen consumption; decreases in lung capacity; and changes in immunologic function. Women who will be beyond the first trimester of pregnancy (greater than or equal to 14 weeks' gestation) during the influenza season should be vaccinated. Pregnant women who have medical conditions that increase their risk for complications from influenza should be vaccinated before the influenza season - regardless of the stage of pregnancy. Because currently available influenza vaccine is an inactivated vaccine, many experts consider influenza vaccination safe during any stage of pregnancy. Some experts prefer to administer influenza vaccination during the second trimester to avoid a coincidental association with spontaneous abortion, which is common in the first trimester, and because exposures to vaccines have traditionally been avoided during the first trimester.

2. Persons Who Should Not Be Vaccinated

a. Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician (see (3)c, Side Effects and Adverse Reactions).

b. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated.

3. Side Effects and Adverse Reactions

a. Because influenza vaccine contains noninfectious killed viruses, it cannot cause influenza. Respiratory disease after vaccination is coincidental and unrelated to influenza vaccination. The most frequent side effect of vaccination is soreness at the vaccination site that lasts up to 2 days. These local reactions generally are mild and rarely interfere with the person's ability to conduct usual daily activities. Systemic reactions have been of two types:

(1) Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6-12 hours after vaccination and can persist for 1 or 2 days.

(2) Immediate, presumably allergic-reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; most reactions likely are caused by residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have developed hives, have had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after eating eggs, should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons with documented immunoglobulin E (IgE) (mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses to egg protein) might also be at increased risk for allergic reactions to influenza vaccine, and consultation with a physician should be considered.

b. Hypersensitivity reactions to any vaccine component can occur. Although exposure to vaccines containing thimerosal can lead to induction of hypersensitivity, most patients do not develop reactions to thimerosal when administered as a component of vaccines, even when patch or intradermal tests for thimerosal indicate hypersensitivity. When reported, hypersensitivity to thimerosal usually has consisted of local, delayed-type hypersensitivity reactions.

c. Although the 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barre′ syndrome (GBS), evidence for a casual relationship of GBS with subsequent vaccines prepared from other virus strains is less clear. However, obtaining strong evidence for a possible small increase in risk is difficult for a rare condition such as GBS, which has an annual background incidence of only 10-20 cases per million adults. During three of four influenza seasons studied from 1977 through 1991, the overall relative risk estimates for GBS after influenza vaccination were slightly elevated but were not statistically significant in any of these studies. However, in a study of the 1992-93 and 1993-94 seasons, the overall relative risk for GBS was 1.7 (95% confidence interval = 1.0-2.8; p=0.04) during the 6 weeks following vaccination, representing an excess of slightly more than one additional case of GBS per million persons vaccinated; the combined number of GBS cases peaked 2 weeks after vaccination. Thus, investigations to date suggest no large increase in GBS associated with influenza vaccines (other than the swine influenza vaccine in 1976) and that if influenza vaccine does pose a risk, it is probably quite small, slightly more than one additional case per million persons vaccinated. Even if GBS were a true side effect of vaccination in subsequent years, the estimated risk for GBS of slightly more than one additional case per million persons vaccinated is substantially less than the risk for severe influenza, which could be prevented by vaccination in all age groups, especially persons aged $\geq$65 years and those who have medical indications for influenza vaccination. The potential benefits of influenza vaccination in preventing serious illness, hospitalization, and death greatly outweigh the possible risks of developing vaccine-associated GBS. The average case-fatality ratio for GBS is 6% and increases with age. However, no evidence indicates that the case-fatality ratio for GBS differs among vaccinated persons and those not vaccinated. Whereas the incidence of GBS in the general population is very low, persons with a history of GBS have a substantially greater likelihood of subsequently developing GBS than persons without such a history. Thus, the likelihood of coincidentally developing GBS after influenza vaccination is expected to be greater among persons with a history of GBS than

among persons with no history of this syndrome. Whether influenza vaccination specifically might increase the risk for recurrence of GBS is not known. Therefore, it would seem prudent to avoid influenza vaccination of persons who are not at high risk for severe influenza complications and who are known to have developed GBS within 6 weeks of a previous influenza vaccination. However, many experts believe that for most persons who have a history of GBS and who are at high risk for severe complications from influenza, the established benefits of influenza vaccination justify yearly vaccination.

d. Hypoprothrombinemia in patients receiving warfarin and elevated theophylline serum concentrations have occurred. Most studies have failed to show any adverse effects of influenza vaccine in patients receiving these drugs. Nevertheless, monitoring for possible enhanced drug effect or toxicity is indicated for those persons taking theophylline preparations or warfarin sodium.

4. Vaccine Dosage. Adult patients should receive one dose in the deltoid muscle of 0.50mL of whole or split virus containing 15 μg each of A/Beijing/262/95-like (H1N1), A/Sydney/5/97-like (H3N2), and B/Beijing/184/93-like hemagglutinin antigens. Beginning each September, influenza vaccine should be offered to persons at high risk when they are seen by health-care providers for routine care or as a result of hospitalization. The months of October through mid-November are optimal for the administration of vaccine since high levels of influenza activity infrequently occur before December in the contiguous United States.

5. Simultaneous Administration of Other Vaccines. The target groups for influenza and pneumococcal vaccination overlap considerably. For persons at high risk who have not previously been vaccinated with pneumococcal vaccine, health care providers should strongly consider administering pneumococcal and influenza vaccines concurrently. Both vaccines can be administered at the same time at different sites without increasing side effects. However, influenza vaccine is administered each year, whereas pneumococcal vaccine is not.

6. Related Preventive Strategies. Antiviral (e.g., rimantadine, amantadine) prophylaxis may be used during an influenza A epidemic in unvaccinated individuals or those who are expected to have an inadequate antibody response to influenza vaccine. Care must be exercised in patients with impaired renal function (especially the elderly) and in patients with seizure disorders if amantadine or rimantadine is used. Chemoprophylaxis is not a substitute for immunization because it does not protect against influenza B. Likewise, compliance for the full 6-12 weeks of an endemic period may be a problem, and it is very costly.

7. VA Medical Center Employees. In recent years many VA medical centers have offered the vaccine to employees (free of charge) because employees may transmit influenza to patients. Influenza vaccine should be offered to employees through the Employee Health Unit for the purpose of protecting patients served by the VA. Immunization records will be maintained in the Employee Health Unit. Expenses involved in this program should be kept at a minimum, and for this reason, the use of centrally-procured vaccine vials is recommended instead of unit dose vaccine.

ATTACHMENT B

VA FORM 10-5549, INFLUENZA VACCINE CONSENT FORM

1. The Disease. Influenza (flu) is caused by viruses. When people get flu they may have fever, chills, headache, dry cough or muscle aches. Illness may last several days or a week or more, and complete recovery is usual. However, complications may lead to pneumonia or death in some people. For the elderly and people with diabetes or heart, lung, or kidney diseases, flu may be especially serious.

2. The Vaccine. Today's flu vaccines cause fewer side effects than those used in the past. In contrast with some other vaccines, flu vaccine can be taken safely during pregnancy; however, flu vaccine should be given to pregnant women according to the chronic illness criteria applied to other persons. One shot will protect most people from influenza during the next flu season.

3. Possible Vaccine Side Effects. Most people will have no side effects from the vaccine. However, tenderness at the site of the shot may occur and last for several days. Some people will also have fever, chills, headache, or muscle aches within the first 48 hours.

4. Special Precautions. As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, flu vaccine has rarely been associated with severe or fatal reactions. An uncommon illness characterized by ascending paralysis (Guillain-Barre′ Syndrome) has been reported following other flu vaccines but not in association with this flu vaccine; however, it must be assumed that the risk is present. Hypersensitivity reactions to any vaccine component can occur. Exposure to vaccines containing thimerosal can lead to induction of hypersensitivity. When reported, hypersensitivity to thimerosal has usually consisted of local, delayed-type hypersensitivity reactions (localized swelling and redness). In some instances people receiving vaccine have had allergic reactions. The following precautions should be carefully noted:

a. People with known allergy to eggs should receive the vaccine only for specific indications and under special medical supervision.

b. People with fever should delay getting vaccinated until the fever is gone.

c. People who have received another type of vaccine in the past 14 days should consult a physician before taking the flu vaccine.

NOTE: Please ask if you have any questions about flu or flu vaccine.

I have read the above statement about influenza (flu), the vaccine, and the special precautions. I have had an opportunity to ask questions, and understand the benefits and risks of flu vaccination. I request that it be given to me or to the person named below of whom I am the parent or guardian.

_____ _____
Name of Person to Receive Vaccine (Please Print) Date Vaccinated

_____ _____
Signature of Person Receiving Vaccine or Parent or Guardian Manufacturer & Lot No.

_____

_____
Date Signed